

Award Number: W81XWH-12-1-0614

TITLE: IN-HOME EXPOSURE THERAPY FOR VETERANS WITH
POSTTRAUMATIC STRESS DISORDER

PRINCIPAL INVESTIGATOR: Leslie Morland, PsyD

CONTRACTING ORGANIZATION: Veterans Medical Research Foundation
San Diego, CA 92161

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14. ABSTRACT We have set up a study that will provide a certain type of exposure therapy, called prolonged exposure therapy (PE) to military Veterans. We will ask 272 Veterans to participate in the study. Our goal is to compare PE conducted in three different ways: (1) PE delivered via office-based telehealth (OBT; Veterans come to the clinic to meet with the therapist over telehealth), (2) PE delivered via home-based telehealth (HBT; Veterans stay at home and meet with the therapist using the computer and video cameras), and (3) PE delivered in home, in person (IHIP; the therapist comes to the Veterans' homes for treatment). We will be checking to see if symptoms of PTSD, depression, and anxiety get better (less severe) after the treatment and six months later. We will also see if there are differences in the three ways we will be providing the therapy. We hypothesize that the IHIP approach, compared to the other two approaches, will be more effective at reducing the PTSD symptoms experienced by these Veterans because it will help Veterans attend each session and complete the therapy "homework" assigned by the therapists (such as doing feared activities around the house or the neighborhood). We have now been referred 814 Veterans. Of the 814 referred, including 654 males (80%) and 160 females (20%), 154 Veterans (19% of those referred) have been randomized to the study. Of the 154 randomized participants, 6 (4%) are currently in Prolonged Exposure therapy, 80 (52%) have completed therapy and 68 (44%) have dropped out of therapy.					
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INTRODUCTION:

This research study provides a type of exposure therapy, called prolonged exposure therapy (PE) to military Veterans. We have proposed to recruit 272 Veterans to participate in the study. Our goal is to compare PE conducted in three different ways: (1) PE that is office-based telehealth (OBT; Veterans come to the clinic to meet with the therapist over telehealth), (2) PE delivered via home-based telehealth (HBT; Veterans stay at home and meet with the therapist using the computer and video cameras), and (3) PE delivered in home, in person (IHIP; the therapist comes to the Veterans' homes for treatment). We will be checking to see if symptoms of PTSD, depression, and anxiety get better (less severe) after the treatment and six months later. We will also see if there are differences in the three ways we will be providing the PE therapy. We hypothesize that the IHIP approach, compared to the other two approaches, will be more effective at reducing the PTSD symptoms experienced by these Veterans because it will help Veterans attend each session and complete the therapy "homework" assigned by the therapists (such as doing feared activities around the house or the neighborhood). However, the delivery of IHIP may cost more than the delivery of PE via the other modalities. We expect that the treatment, conducted in all three ways, will reduce the distress caused by PTSD symptoms in most of the participants, which will help to improve the lives of Veterans, their families, and society. The findings of this study will also benefit military Veterans and Active Duty military personnel by investigating new ways for treating PTSD so that the most effective treatments can be made widely available. We will also learn the best ways to manage urgent situations, such as a physical or emotional crisis, that occur when providing treatment in homes and through home based video technology.

BODY:

Our focus in the past year (30 Sept 2015 – 29 Sept 2016) has been to accomplish the tasks outlined in the new Statement of Work (SOW) under Tasks 2. Namely, we continue to recruit from multiple clinic sites, meet with clinical staff, and San Diego VA Veterans to introduce the project, establish liaisons, and generate referrals. The study staff has been actively receiving referrals and scheduling interviews. We have significantly increased our recruitment this past year through aggressive recruitment efforts within the VA hospital and community-based outpatient clinics, resulting in an increase in referrals to the project.

We continue to use our developed recruitment materials, including brochures and flyers, and we use internal advertisements for the project (e.g., newsletters, messages on VA TVs and VA website). We have developed a feedback loop to determine the primary recruitment sites with positive referrals for the project and then use this information to refine our recruitment strategy and efforts.

Assessment clinicians are actively administering IRB approved informed consent and conducting comprehensive baseline assessments with potential participants as well as assessments at post-treatment and follow-up. We have used the randomization scheme developed by the study statistician to randomize eligible participants to therapy. The Clinician-Assessed PTSD Scale for DSM-5 (CAPS-5) assessment fidelity procedures are underway, per study protocol.

Our treatment clinicians are providing the manual-guided evidence-based PE PTSD intervention. Therapists attend a weekly PE Consultation Team meeting with Dr. Peter Tuerk. PE fidelity procedures are underway, per study protocol.

We have weekly in person research meetings with our local study personnel, a separate meeting for the assessment team, and another meeting for research assistants. Our foremost concern is safety, and we will have ongoing discussions about ways to maximize safety of Veterans and therapists in all three conditions. We continue to meet bimonthly with the parallel study examining home-based CPT lead by Drs. Resick and Peterson with the plan to compare and potentially collapse findings as feasible.

The study database is complete and study staff are overseeing data entry and quality control conducted by research assistants and study staff. We are using the study database to enter study data collected at different assessment and treatment time points. All data inputting is occurring in real time with rigorous quality control procedures in place.

We have completed five pilot subjects. These pilot sessions helped us refine our procedures for recruitment, telephone screening, consent, assessment, the home-based modalities, and treatment. We presented some anecdotes from this study at the International Society for Traumatic Stress Studies (ISTSS) annual meeting in November of 2015 (see full reference below). We also have a manuscript in press and two manuscripts in preparation (see full references below). One is based on what we learned from our pilot subjects, entitled *A pilot study of home-based psychotherapy for posttraumatic stress disorder* under review and the other is based on Veterans report of preferences for care.

For the full project sample, we have been referred 814 Veterans. Of the 814 referred, including 654 males (80%) and 160 females (20%), 278 were fully screened over the phone. Of the 278 individuals who were fully screened, 182 were assessed and consented at the baseline assessment. 159 of these individuals were eligible (20% of those referred) but 5 were selected as pilot cases and 154 Veterans have been randomized to the study. Of the 154 randomized participants, 6 (4%) are currently still active in Prolonged Exposure therapy, 80 (52%) have completed therapy, and 68 (44%) have dropped out of therapy. We continue to recruit and offer 6 PE therapy slots a week.

The 68 who dropped out included 16 (23%) who reported not feeling able to continue with the imaginal exposure component of treatment, 15 (22%) who stopped attending their therapy sessions for unknown reasons and did not respond to phone calls and letters from study personnel, 10 (15%) who could not commit to a weekly treatment schedule, 5 (7%) who relocated during treatment, 2 (3%) who dropped out after being randomized but never began treatment, 8 (12%) who had severe health concerns arise during treatment, and 12 (18%) who cited other reasons.

Of the 814 referred, 655 (80% of the total referred) have not been enrolled. Of those not enrolled, 1 Veteran (0.1% of those not enrolled) has not yet been contacted, and contact is in progress with 5 Veterans (1%). Another 96 Veterans (15%) were not enrolled into the study because they were unreachable by phone (no response after 6 voice messages). A total of 247 Veterans (38%) were ineligible for study inclusion after completing the phone screen; 240 Veterans (36%) were not interested in joining the study; 11 Veterans (2%) are on a hold (either waiting for their current PTSD treatment to end, waiting to be on a stable dosage of medications for two months, or waiting for personal reasons such as vacation or surgery); 5 Veterans (1%) are eligible for assessment and scheduling for baseline assessment is underway; 27 Veterans (4%) were eligible after the phone screen, but contact was lost before baseline assessment could be scheduled; and a total of 23 Veterans (3%) were initially eligible at phone screen, but found ineligible for study inclusion after the baseline assessment.

The remaining 154 Veterans (97%) were randomized into the full study. Of those randomized, 6 (4%) are currently enrolled in PE treatment; 13 (9%) have completed PE treatment and have moved into the follow-up phase of the study (post through 6 month); 19 (12%) have completed PE treatment through 6 month follow-up, but have at least one missing follow-up assessment; 48 (31%) have completed all PE treatment and all post assessments; and a total of 68 (44%) have dropped out of treatment. Of the drop outs, 27 (40%) have dropped out of PE treatment, but are being seen for follow-up assessments; 25 (37%) have dropped out of PE treatment and have closed follow-ups with at least one follow-up assessment completed; 16 (23%) have dropped out of PE treatment and their follow-ups are closed with no follow-up assessment completed.

Of the 154 who were randomized, 111 (72%) are male and 43 (28%) are female. The racial/ethnic information for the 154 randomized Veterans is as follows: 43 (28%) identify as African American, 13 (8%) identify as Asian, 64 (42%) identify as Caucasian, 5 (3%) identify as American Indian or Alaskan Native, 4 (3%) identify as Native Hawaiian or Other Pacific Islander, 10 (6%) declined to answer, and 15 (10%) reported "Other".

The randomization breakdown for the 154 Veterans enrolled into PE treatment is as follows: 51 (33.1%) were randomized to receive In-Home, In-Person (IHIP); 51 (33.1%) were randomized to receive Office-Based Telehealth (OBT); and 52 (33.8%) were randomized to receive Home-Based Telehealth (HBT).

KEY RESEARCH ACCOMPLISHMENTS:

We have obtained VA San Diego IRB and R&D Approval to conduct our study (IRB #H130390). HRPO has provided initial approval (and most recent re-approval in August 2016).

We have hired all personnel, and have completed training with all personnel. Due to a reduced staff in this last phase of the study we have now 2 part time clinicians who offer PE treatment for this study.

We continue to consult with national experts about in-home provision of care (through teleconferencing and in-person).

We have purchased equipment and supplies for the project and prepared paperwork (including recruitment materials).

We created an Access Database for study data entry and all data that has been collected over the past 4 years has been input. This now allow for data analyses to occur using baseline data and once the study is complete the final analyses and publication will be completed swiftly at the final stage of this study.

REPORTABLE OUTCOMES:

- *Publication/presentations:*
 - **Morland, L. A.**, Wells, S. Y., Howard, I. C., Mikhael, T., Savage, U., Tunze, C. A., Sohn, M., Walter, K. H., & Thorp, S. R. (2015, November). *Preliminary findings from a study of home-based psychotherapy for posttraumatic stress disorder*. Poster presented at the 31st Annual International Society for Traumatic Stress Studies (ISTSS), New Orleans, LA.
 - **Morland, L. A.**, Wells, S. Y., Glassman, L. H., Grubbs, K. M., Savage, U., Golshan, S., Thorp, S. R., & Acierno, R. (**in preparation**). Veterans'

preferences for PTSD treatment delivery modality.

- Thorp, S. R., Morales, J. S., Wells, S. Y., Glassman, L. H., Moreno, L., Walter, K. H., Howard, C., **Morland, L., A., & Acierno, R. (in preparation)**. A pilot study of home-based psychotherapy for posttraumatic stress disorder.
- patents and licenses applied for and/or issued;
 - None
- degrees obtained that are supported by this award;
 - None
- development of cell lines, tissue, or serum repositories;
 - N/A
- informatics such as databases and animal models, etc.;
 - An Access Database has been created for use of the present study data entry.
- funding applied for based on work supported by this award;
 - Awarded the Frank W Putnam Trauma Research Scholar award from the International Society for Traumatic Stress Studies to help fund student Stephanie Wells'; dissertation project which will involve conducting qualitative interviews with participants following their completion of this study.
- employment or research opportunities applied for and/or received based on experience/training supported by this award.
 - None

CHALLENGES:

In this past year of this study we had several challenges. The primary project PI, Steven Thorp, left the VA and the study somewhat abruptly at the end of year 3. The existing research team, having discovered procedural errors implemented by Dr. Thorp, asked Dr. Morland to assume the role of primary PI in year 4. Early in year 4, Dr. Morland secured a small cost extension for a 5th year to allow us to continue to enroll new participants through the end of year 4 and then complete all follow-up assessments and dissemination efforts in year 5. However in the past year we were significantly impacted during the second half of the project year by the **VA Choice program**, which is a VA program that has been temporarily implemented to address the access issue and the inability of the VA to meet the demands of patient care. In most cases, this VA Choice program resulted in rerouting all new Veterans seeking care into the community rather than through VA San Diego PTSD clinics. This significantly slowed referrals for all studies across the VA over the past 6 months. Although our study continues to receive a slow but steady flow of referrals and we made screening and randomization our top priority, we did not accomplish the target enrollment we anticipated this past year. The VA Choice program appears to have been fraught with problems of its own, and Veterans are returning to the VA for their mental health care. At this stage we have determined that we will continue recruitment into the first quarter of the 5th year and if necessary potentially complete final assessments into an extended 6th year. This will allow us to increase the amount of participants we see in this study and allow our study to enroll and randomize toward the projected participant recruitment goals, as stated under Task 2, Statement of Work. However given the lack of funds for therapist time in year 5 we have secured 2 non-DOD funded therapists that give us 6 slots a week. With these non-DoD in kind resources, and remaining DOD resources, we anticipate enrolling an additional 16 participants in the next quarter to bring us to a sample size of 175 total participants, including the 5 pilot cases, instead of the initially proposed 272 (**See submission of request for revised SOW and justification for modification to SOW**). In consultation with our statistician we have determined that with this sample size we anticipate being adequately powered to address all of the hypotheses looking at *superiority* and difference between treatment arms. One change is that our *Hypotheses 1b states that there will be no difference between the HBT and OBT modalities on reduction in PTSD symptoms*. We initially proposed to address this hypothesis with a non-inferiority analysis. However given the reduced sample size we are now proposing to

address this hypothesis through conducting overall ANOVA analyses with post hoc comparison between treatment arms to determine any difference between arms. These analyses will allow us to address the a priori established hypothesis of superiority, but will not allow us to conduct true non inferiority analyses, which are based not on lack of significant between group differences, but rather on lack range differences with respect to a priori effect size confidence interval specification. In other words, we will examine comparability between groups using statistical significance or lack thereof, rather than effect size confidence intervals overlaid on a pre specified range of non-inferiority (e.g., we will use statistical testing via ANOVA to derive conclusions of 'lack of difference', rather than "treatment A is as good as treatment B as long as the confidence interval of the effect size does not fall below x number of points on the PCL".

CONCLUSION

At the end of year 4 of this study we have enrolled 58.5% of the projected sample size and we are making slow progress toward recruitment goals. In this past year we have enrolled over 31% of our total participants and have actively input all baseline and post assessment data into the database. Our data base is clean and all fidelity is on track and we anticipate being prepared to publish immediately following the completion of the final assessments with a new proposed sample size.

REFERENCES:

None

APPENDICES:

None

Revised Statement of Work

Project Title: “In-Home Exposure Therapy for Veterans with PTSD” Primary Institution:
Department of Veteran Affairs
VA San Diego Healthcare System (VASDHS)
3350 La Jolla Village Drive, San Diego, CA 92161

Clinical Sites:

VA San Diego Healthcare System (parent facility), which includes:

- VA San Diego Healthcare System (VASDHS)
Address: *3350 La Jolla Village Drive, San Diego, CA 92161*
- Veterans Medical Research Foundation (VMRF)
Address: *3350 La Jolla Village Drive, San Diego, CA 92161*
- Mission Valley Outpatient Clinic
Address: *8810 Rio San Diego Drive, San Diego, CA 92108*
- Chula Vista Outpatient Clinic
Address: *835 Third Ave, Chula Vista, CA 91910*
- Oceanside Outpatient Clinic
Address: *1300 Rancho Del Oro Dr, Oceanside, CA 92056*
- Escondido Outpatient Clinic
Address: *815 E Pennsylvania Ave, Escondido, CA 92025*

Justification for modification:

Over the past several years studies have demonstrated that clinical videoconferencing technology (CVT) can achieve comparable clinical outcomes to office-based, in-person delivery of care across various therapies with diverse patient populations (Backhaus et al., 2012). Randomized clinical trials (RCTs) have demonstrated that PTSD outcomes with CVT delivery of trauma-focused therapies are comparable to outcomes associated with traditional service delivery methods. These specific RCTs often employ a noninferiority methodological approach. Studies have included a recent RCT conducted with Veterans with PTSD confirming the noninferiority of using CVT to deliver an evidence-based treatment (EBT) for PTSD, Cognitive Processing Therapy (CPT; Resick et al., 2007), relative to CPT delivered in-person (Morland et al., 2014; Morland et al., in press). A pilot study of Prolonged Exposure (PE; Foa, Hembree, & Rothbaum, 2007) delivered via CVT to Veterans with PTSD evidenced significant decreases in clinical outcomes and provided support for the feasibility and safety of trauma-focused treatments delivered via CVT (Tuerk, Yoder, Ruggiero, Gros, & Acierno, 2010). A recent RCT (Fortney et al., 2015) found that a collaborative care model, which included treatment with CPT, medication and case management, and psychiatric consultations delivered via telehealth, produced larger reductions in PTSD symptoms compared to outcomes found in the treatment-as-usual condition (and thus, enhanced treatment engagement and increased access to and delivery of EBTs relative to usual care).

Veterans with PTSD have shown high degrees of patient and clinician satisfaction with CVT (Deitsch, Frueh, & Santos, 2000) and rates of attendance (Greene et al., 2010) comparable to in-person care in other CVT studies. Furthermore, research investigating therapist effects in CVT indicates that therapist adherence (Morland et al., 2011), therapist competence, and therapist fidelity when delivering manualized treatment protocols is similar in CVT and in-person modalities (Frueh et al., 2007).

Due to the literature supporting the equivalence of office-based CVT modalities for provision of EBPs, CVT services have been disseminated broadly across VHA and are currently reimbursed comparable to face-to-face traditional care. Provision of services using an office-based CVT modality is very much the new standard of care in the VA and allows providers to extend their clinical reach and increase access without reducing quality of care. Therefore, as stated this is an appropriate control arm for our current In-home PE study which examines the advantages of providing services in the home as compared to an office based control. In addition, there is some

added value in having a different control group than the parallel DoD/CDMRP study (comparing modalities of treatment for CPT).

Additional Study/Subaward Sites: None. Table 1, Summary of Tasks:

Year 1	Task 1	Q1	Months 1-3
		Q2	Months 4-6
	Task 2	Q3	Months 7-9
		Q4	Months 10-12
Year 2		Q5	Months 13-15
		Q6	Months 16-18
		Q7	Months 19-21
		Q8	Months 22-24
Year 3		Q9	Months 25-27
		Q10	Months 28-30
		Q11	Months 31-33
		Q12	Months 34-36
Year 4		Q13	Months 37-39
		Q14	Months 40-42
	Q15	Months 43-45	
	Q16	Months 46-48	
Year 5	Task 3	Q17	Months 49-51
		Q18	Months 52-54
	Task 4	Q19	Months 55-57
		Q20	Months 58-60

Task 1. Attain regulatory review and approval; Assemble and train core research team (Months 1-6, includes Quarters (Q) 1-2, see details below):

- a. Core project staff will be hired and oriented to the project (Q1 – Q2).
- b. Project team will be trained on regulations concerning the use of human subjects, clinical safety, and confidentiality. They will be given an overview of the project and an understanding of the role each member plays (Q1 – Q2).
- c. Treatment clinicians will be trained to use the video conferencing (VTC) modality and how to respond to technical difficulties (Q1 – Q2).
- d. Treatment clinicians will be trained to conduct the standardized PE protocol at acceptable levels of adherence and competence (Q1 – Q2).
- e. Assessment clinician will be trained to conduct baseline pre-treatment, post-treatment and 6-month follow-up assessments (Q1 – Q2).
- f. Project coordinator and statisticians will develop procedures for data entry and data management (Q1 – Q2).
- g. Clinical supervisors will establish fidelity monitoring procedures including videotaping of all treatment sessions to monitor adherence to protocol (Q1 – Q2).
- h. Begin recruitment. Number of research subjects required for Task 1: 0 enrollees (Q2; recruitment commenced).

Task 2. Enroll participants and begin treatment (Months 7-48, includes Quarters (Q) 3-16, see details below):

- a. Participants will be recruited from multiple clinical sites (Q3 – Q16).
- b. Develop recruiting materials such as information flyers for patients and providers (Q3 – Q4).
- c. Meet with clinical staff at sites to introduce project, establish site liaisons, and generate referrals. (Q3 – Q4)
- d. Interested participants will be referred to research team staff and interviews scheduled (Q3 – Q16).
- e. Assessment clinicians will administer informed consent and conduct comprehensive baseline assessment with potential participants. (Q3 – Q16)
- f. Participants who meet the study's inclusion criteria will be randomized into either the in-person delivery of PE (IHIP) condition, the office-based telehealth (OBT) condition, or the home-based telehealth (HBT) condition. A statistician who is blind to participant identities will conduct the randomization. **175** participants will be randomized in 1 of 3 conditions (IHIP, OBT, or HBT). (Q3-Q15)
- g. Treatment clinicians will conduct a manual-guided evidence based PTSD intervention, Prolonged Exposure Therapy (PE), with approximately **175** enrolled participants, for a total of **149** Veterans, Reserve & Guard who have completed the treatment (takes into account the approximately **14.8%** overall attrition: **10%** attrition for in-home care and **20%** for office-based and home-based telehealth care.) (Q3-Q16)
- h. Each condition will contain a minimum of enrolled Veterans, Reserve & Guard as follows: approximately **55** participants for in-home care (IHIP) and approximately **60** participants for office-based telehealth (OBT) and approximately **60** participants for home-based telehealth care (HBT) and will meet once a week for 12 weeks. (Q3 – Q16)
- i. Veterans, Reserve & Guard will be recruited and assessed to determine eligibility. Of the potential participants assessed we will enroll and randomize **175** participants. With an overall **14.8%** attrition we anticipate **149** participants will complete the treatment. We will conduct initial assessments and treatment at the VA San Diego Healthcare System. The office-based telehealth (OBT) therapy will take place in the Veterans Medical Research Foundation (VMRF) building, based in San Diego, CA (on the same campus as the VA Medical Center and the University of San Diego) and in the offices of the VA San Diego Healthcare System (VASDHS) Mission Valley

Outpatient Clinic. (Q3 – Q16)

- j. Assessment clinicians will conduct in-person assessments at post-treatment and 6 months post treatment, as well as phone assessments at 2 months and 4 months post treatment. Assessments will collect clinical data (e.g. symptom severity). (Q6 – Q16)
- k. Research and administrative assistants will conduct data entry. Project coordinator will oversee and conduct reliability checks. (Q1 – Q16)
- l. Clinicians will receive weekly supervision. (Q1- Q16)
- m. Core project team will meet weekly, with monthly extended team meetings. (Q1 – Q16)
- n. Number of research subjects required to complete Task 2: **175** enrollees (recruitment, treatment and follow-up assessments ongoing). (Q3-Q16)

Task 3. Complete delayed final assessments (Months 49-54, includes Quarters 17-18, see details below):

- a. Assessment clinician will conduct assessments at 6 month post-treatment to determine maintenance of treatment effects. (Q17-18)
- b. Number of research subjects required to complete Task 3: **175** enrollees (recruitment completed, treatment and follow-up assessments ongoing).
- c. Quarter 17
 - 1. Continue recruitment
 - 2. Treatment complete
 - 3. Follow-up interviews ongoing
- d. Quarter 18
 - 1. Recruitment complete
 - 2. Treatment complete
 - 3. Continue follow-up interviews

Task 4. Conduct data analysis, complete final report and manuscripts and disseminate study findings (Months 55-60, includes Quarters 19-20, see details below):

- a. Investigators will conduct preliminary descriptive analysis. (Q19 – Q20)
- b. A superiority analysis (and secondary non-inferiority analysis) will be used to test the primary hypothesis that the in home, in person delivery of PE (IHIP) will demonstrate greater reductions in the severity of symptoms of PTSD from pre- to post-treatment and from pre-treatment to 6-month follow-up relative to the office-based telemedicine (OBT) or home-based telehealth (HBT) modalities, and OBT and HBT will not differ significantly from each other (lack of difference testing). (Q19-20)
- c. Principal investigator will visit each remote site to initiate wrap up activities for the active treatment. (Q19)
- d. Core project staff will create a research manuscript to be submitted to a suitable research journal for publication. (Q19-20)
- e. **Project PI will continue collaborations with our parallel in-home study (CPT; Co-PIs Drs. Peterson and Resick) and will specifically work to develop a shared data repository in this last phase of the study that includes both study databases (Q19-20). Identify specific publications that can maximize on the collaborative database effort.**
- f. Written materials will be distributed through the VA website and the VA Care Coordination Telemental Health Leadership Group. (Q19)
- g. Investigators will present the project's key findings at a suitable research conference. (Q20)
- h. Number of research participants required to complete Task 4: 0 (recruitment, treatment and follow-up assessments completed).
- i. Quarter 20
 - a. Recruitment complete (**175** participants enrolled)
 - b. Treatment complete for all participants (**149** participants complete)
 - c. Follow-up interviews complete for all participants

Award Number: W81XWH-12-1-0614

TITLE: In-Home Exposure Therapy for Veterans with PTSD

PRINCIPAL INVESTIGATOR: Leslie Morland, PsyD

CONTRACTING ORGANIZATION: Veterans Medical Research Foundation
San Diego, CA 92161

TYPE OF REPORT: Justification for SOW modification

DATE: December 23, 2016

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

JUSSTIFICATION FOR MODIFICATION TO SOW:

We are requesting a modification to our SOW specifically to target enrollment at 175 instead of 272. Early in year 4, Dr. Morland secured a small cost extension for a 5th year to allow us to continue to enroll new participants through the end of year 4 and then complete all follow-up assessments and dissemination efforts in year 5. However in the past year we were significantly impacted during the second half of the project year by the **VA Choice program**, which is a VA program that has been temporarily implemented to address the access issue and the inability of the VA to meet the demands of patient care. In most cases, this VA Choice program resulted in rerouting all new Veterans seeking care into the community rather than through VA San Diego PTSD clinics which impacted recruitment. This significantly slowed referrals for all studies across the SDVA over the past 6-12 months. Although our study continues to receive a slow but steady flow of referrals and we made screening and randomization our top priority, we did not accomplish the target enrollment we anticipated this past year. At this stage with our limited funds and time we have determined that we will continue recruitment into the first quarter of the 5th year and if necessary potentially complete final assessments into an extended 6th year. This will allow us to increase the amount of participants we see in this study and allow our study to enroll and randomize toward the new projected participant recruitment goals of 175, as stated under Task 2, of the modified Statement of Work. However given the unanticipated delays in enrollment as well as lack of funds for therapist time we are requesting a modification to our targeted sample size from 272 to 175. In consultation with our statistician we have determined that with this sample size of 175 we anticipate being adequately powered to address all of the hypotheses looking at *superiority* and difference between treatment arms. One change is that our *Hypotheses 1b states that there will be no difference between the HBT and OBT modalities on reduction in PTSD symptoms*. We initially proposed to address this hypothesis with a **noninferiority analysis**. However given the reduced sample size we are now proposing to address this hypothesis through conducting overall ANOVA analyses with post hoc comparison

between treatment arms to determine any difference between arms. These analyses will allow us to address the a priori established hypothesis of superiority, but will not allow us to conduct true noninferiority analyses, which are based not on lack of significant between group differences, but rather on lack of range differences with respect to a priori effect size confidence interval specification. In other words with the reduced sample size, we will examine comparability between groups using statistical significance or lack thereof, rather than effect size confidence intervals overlaid on a pre specified range of non-inferiority (e.g., we will use statistical testing via ANOVA to derive conclusions of 'lack of difference', rather than "treatment A is as good as treatment B as long as the confidence interval of the effect size does not fall below x number of points on the PCL".

In conclusion, we are optimistic that we can accomplish the goals on the modified SOW, if approved, and delivery on our overall project goals.